in Guatemala should be prioritized for vaccination.

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Adjuvanted influenza vaccines and their potential role for vaccination of travelers

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Background: Trivalent seasonal influenza vaccine (TIV) adjuvanted with the emulsion adjuvant MF59® (FLUAD®) is licensed in 29 countries worldwide for adults over 65 years of age. Compared with unadjuvanted TIV, the adjuvanted vaccine provides higher hemagglutination inhibition (HI) antibody titers not only against vaccine strains, but also against drift-variant strains. Usually influenza is transmitted in a single epidemic seasonal epidemic in temperate climates, but it may appear in two epidemics during the year or may be transmitted throughout the year, in subtropical and tropical locations. Although persons travelling from the Northern Hemisphere (NH) to the tropics or antipodes may not have access to the TIV made with strains used in the Southern Hemisphere (SH) formulation, they are nevertheless recommended to receive available NH formulation-TIV because one or more of the strains may overlap and because some degree of protection may be elicited, even by an imperfectly matched vaccine.

Methods: The following data from recent clinical trials highlight the cross-protection elicited by the MF59-adjuvanted vaccine. Sera from 222 children, 6-36 months of age, vaccinated with the 2006/07 formulations of FLUAD or unadjuvanted TIV were tested against the H1N1 strain in the 2007/08 formulation (A/Solomon Islands/3/2006 (H1N1)-like). Sera from adults with chronic illnesses and elderly adults (> 65 years) were similarly tested.

Results: In the children geometric mean titer (GMT) HI responses, geometric mean ratios (GMR), and seroprotection (SP) rates were significantly higher in FLUAD recipients. Similar significant differences were seen among 349 adults with chronic illnesses with increased risk for influenza morbidity who were vaccinated with either FLUAD or with an undajuvanted subunit vaccine. Finally, 56 elderly adults who received the 2007/08 FLUAD formulation displayed postvaccination responses against strains in the 2008/09 formulation which met the European Committee for Human Medicinal Products criteria for GMR, SP and SC for the mismatched H1N1 and H3N2 strains.

Conclusion: Altogether these results suggest that the greater degree of cross-variant immunity elicited by MF59-adjuvanted influenza vaccine may offer an advantage in circumstances where travelers may be exposed to antigenically mismatched viruses.

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Seasonal influenza vaccine may be associated with increased risk of illness due to the 2009 pandemic A/H1N1 virus

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Background: In late spring 2009, concern was raised in Canada that prior receipt of the 2008-09 trivalent inactivated influenza vaccine (TIV) was associated with increased risk of pandemic H1N1 (pH1N1) illness. Several epidemiologic investigations were urgently conducted through the summer to assess this putative association.

Methods: Studies included: (1) test-negative case-control design based on Canada's ongoing sentinel vaccine effectiveness monitoring system in British Columbia, Alberta, Ontario and Quebec; (2) conventional case-control design using population controls in Quebec; (3) testnegative case-control design in Ontario and (4) prospective household transmission (cohort) study in Quebec. Logistic regression estimated odds ratios for TIV effect on community- or hospital-based laboratory-confirmed seasonal or pH1N1 influenza cases compared to controls with restriction, stratification and adjustment for covariates including combinations of age, sex, comorbidity, timeliness of medical visit, prior physician visits, and/or health care worker status. For the prospective study relative risks were computed.

Results: Based on the sentinel study of ~700 cases and 900 controls, 2008-09 TIV provided statistically significant protection against seasonal influenza (OR 0.44;95% CI 0.33-0.59). Conversely, estimates from the sentinel and several other study designs involving ~1200 laboratory-confirmed pH1N1 cases and 1500 controls consistently showed that prior recipients of 2008-09 TIV were at statistically significant 1.5-2.5-fold increased risk of medically-attended pH1N1 illness during the spring/summer 2009 with upper limit of the 95% confidence interval spanning 3-4-fold increase. There was non-significant increase in the strength of the association with more TIV doses received in the prior five years. Risk of pH1N1 hospitalization was not further increased among vaccinated people when comparing hospitalized to community cases.

Conclusion: Prior receipt of 2008-09 TIV was associated with increased risk of medicallyattended pH1N1 illness during the spring/summer 2009 in Canada. Possible biologi-

cal mechanisms and immuno-epidemiologic implications are considered.

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Monitoring for avian influenza in wild birds on the Far East in 2008

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Background: Waterbirds are natural reservoirs for low-pathogenic avian influenza and have been implicated as the primary source of infection in outbreaks of highly pathogenic avian influenza. An understanding of the movements of birds and the ecology of avian influenza viruses within the wild bird population is essential in assessing the risks to human health and production industries. The purpose of this investigation was surveillance for avian influenza in migratory shorebirds at the East Asian-Australasian Flyway. Sample collection was on Kamchatka, on the Kuril islands, at the Amursky region, on Sakhalin and on Chukchi Peninsula.

Methods: Viral RNA was isolated from virus-containing allantoic fluid with the RNeasy Mini kit (QIAGEN, Valencia, CA, USA) as specified by the manufacturer. Uni12 primer was used for reverse transcription. PCR was performed with a set of primers specific for each gene segment of influenza A virus (*18*). PCR products were purified with the QIAquick PCR purification or QIAquick gel extraction kit (QIAGEN). The amplicons were sequenced on an automated Applied Biosystems 3130 system using BigDye terminator cycle sequencing ready reaction kit» (Applied BioSystems).

Results: In the Far East in the 2008 from birds of 127 spices and 32 families were collected 4248 samples and 16 influenza viruses were isolated and analyzed. No highly pathogenic avian influenza viruses were identified. The hemagglutinin genes of stains A/Larus/Kamchatka/521/08(H13N6) isolated in Kamchatka region and A/Teal/Tinda/6114/08(H10N6) (bankit1288867 in genebank) isolated in Amursky region were analyzed genetically. The analysis shows homology with the strains which were isolated in the Astrahansky region and on Hokkaido island.

Conclusion: Surveillance activities for avian influenza in wild birds should be continued to provide further epidemiological information about circulating viruses and to identify any changes in subtype prevalence.

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Influenza surveillance contributions from South and Southeast Asia

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Background: On-going, comprehensive influenza surveillance is critical to detect and monitor influenza outbreaks. The Armed Forces Research Institute of Medical Sciences (AFRIMS) has established 45 influenza sentinel sites in South and Southeast Asia in 4 countries (Thailand, Nepal, Philippines, Bhutan) and an additional 9 countries with participating US Embassies.

Methods: Patients who present with a history of fever and cough or sore throat can participate. Samples are tested with a rapid test for influenza A and B and realtime PCR for influenza A (H1, pH1, H3, H5) and B. Some positive samples undergo virus isolation, characterization and sequencing at AFRIMS or in the US at the Centers for Disease Control and Prevention (WHO Collaborating Center for Surveillance, Epidemiology and Control of Influenza).

Results: From October 2005 through September 2009, AFRIMS sites collected samples from 7,713 patients with 4,239 taken since the H1N1 outbreak started in May 2009. For the entire surveillance period, 42.2% of the samples were positive for influenza A or B by PCR. Since June 2009, 39.1% of the positive influenza samples have been pH1N1 positive. Our surveillance system was the first to detect the presence of pH1N1 in Nepal and Bhutan. Evaluation of influenza rapid tests compared to PCR differed by site but had overall 60% sensitivity and 97% specificity, and pH1N1 had a 68% sensitivity and 98% specificity. Sequences from recent seasonal H1N1 viruses demonstrated greater than 97% homology at the amino acid level with the 08/09 H1N1 vaccine strain. Samples from Bhutan and the Philippines had a very similar strain in circulation with 98.9-99.6% homology at the amino acid level. A/Nepal/NP06C-017/2008 showed the greatest divergence with the other strains (96.6-97.5% homology). Seven pandemic H1N1 HA genes were sequenced and compared to other circulating viruses and were very similar. To date, all seasonal H1N1 and H3N2 viruses that have been screened have genetic markers for M2 blocker resistance and all pH1N1 demonstrate NA inhibitor resistance.